AN IN SILICO APPROACH TOWARDS INHIBITION OF DENGUE VIRUS ENTRY USING CD209 IN DENDRITIC CELLS AS TARGET

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CERTIFICATE

This is to certify that the thesis entitled "**An In Silico Approach Towards Inhibition Of Dengue Virus Entry Using CD209 In Dendritic Cells As Target**" submitted by Sri Mahesh Rajbeer Nagwan (Roll No. 110BT0546) in partial fulfilment of the requirements for the award of Bachelor of Technology degree in Biotechnology at the National Institute of Technology, Rourkela is an authentic work carried out by him under my supervision and guidance.

To the best of my knowledge, the matter embodied in this thesis has not formed the basis for the award of any Degree or Diploma or similar title of any University or Institution.

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ABSTRACT

Dengue virus (DENV) infections are expanding worldwide and, because of the lack of a vaccine, the search for antiviral products is imperative. It would be interesting to develop

an antiviral product that can interact with dengue virus(DENV) or its receptor, prevent host cell infection and subsequent immune activation. DENVentry is thus an interesting target for antiviral therapy. DENV enters the host cell through receptor-mediated endocytosis. Several cellular receptors have been proposed, and DC-SIGN(CD209), present on dendritic cells, is considered as the most important DENVreceptor until now. Because DENV entry is a target for antiviral therapy, various classes of compounds have been investigated to inhibit this process. The Carbohydrate Binding Agents(CBAs) are considered effective against inhibiting viral entry into the host cell.

In this project, various CBAs like *Hippeastrum hybrid* (HHA), *Galanthus nivalis* (GNA), and *Urtica dioica* (UDA) along with their analogues are used as ligands for the DENV receptor present on the dendritic cells (DCs). Using AutoDock vina, we find their binding energy with the receptor and thus determine an effective CBA and hence a potential drug against the desease. The UDA molecule shows high affinity for the DC-SIGN(CD209) receptor and hence can be used as an effective drug.

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CHAPTER 1

INTRODUCTION

1. INTRODUCTION

Dengue virus is an expanding public health problem in tropical and subtropical regions of the world, mainly owing to failure in the maintenance of control programs for the mosquito vector *Aedes aegypti* and increasing and unplanned urbanization. It has been estimated that over 50 million dengue virus infections of varying severity occur globally each year, making this virus the most significant mosquito-borne human pathogen.

Dengue virus (DENV) is a single-stranded, positive-sense enveloped RNA virus of the *Flaviviridae* family that is transmitted by *Aedes aegypti* and *Aedes albopictus*. There are four antigenically related but distinct serotypes of dengue virus, designated DEN-1, DEN-2, DEN-3, and DEN-4, and infection by any one serotype does not protect the individual from infection by the remaining three serotypes. Each serotype shares around 65% of the genome, and, despite of the differences, each serotype causes nearly identical syndromes in humans and circulates in the same ecological niche . Dengue virus causes clinical syndromes in humans, ranging from an acute self-limited febrile illness (dengue fever, DF) to a severe and life-threatening vascular leakage and shock (dengue hemorrhagic fever/dengue shock syndrome, DHF/DSS). It has been postulated that hemorrhagic fever or shock syndrome is usually the result of sequential infection with multiple serotypes In the last decade, due to a decline of vector control efforts, DENV has reemerged in tropical areas and is considered as the most common arthropod-borne tropical disease that endangers an estimated 2.5 billion people. Every year, 50 million infections occur, including 500,000 hospitalizations for DHF, mainly among children, with a case fatality rate exceeding 5% in some areas.

Despite the importance and increasing incidence of DENV as a human pathogen, there are no antiviral agents or vaccines available for treatment or prevention, and little is known about the cell biology or the life cycle of DENV in mosquitos or mammalian cells. The development of a successful chemotherapy for DENV infection requires a better understanding of the viral life cycle to elucidate potential targets and, thus, to obtain key information for the rational design of antiviral drugs.

1.1.1 Structure Of Dengue Virus

The dengue virus surface is composed of 180 copies of the envelope glycoprotein and the membrane protein. The E protein of dengue virus contains a class II fusion peptide sequence that is important for viral invasion of a host cell. There are remarkable structural deviations between the immature and mature dengue envelopes as revealed by elegant cryo-electron microscopy studies. The immature dengue virus particle is covered with 60 asymmetric trimers of prM-E heterodimers that stick out like spikes from its surface. The prM protein protects E from premature fusion while passing through the acidic environment of the trans-Golgi network (TGN) during morphogenesis. During maturation, the Nterminal part of the prM protein is released by the host cell furin that induces a rearrangement of the E proteins essential for fusion. In the mature virus, the E proteins exist as homodimers that lie on the viral membrane in the form of 30 so-called "rafts". Each raft contains three parallel dimers arranged in icosahedral symmetry and organized into a herringbone pattern.

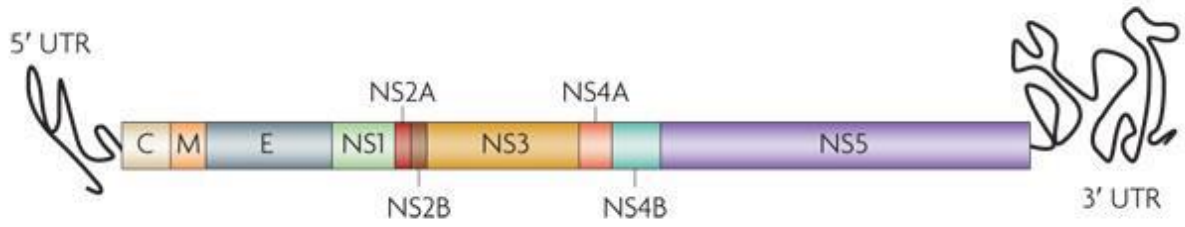


Figure 1 Structure of a dengue virus

CHAPTER 2

LITERATURE REVIEW

2. LITERATURE REVIEW

2.1 Mechanism Of Dengue Virus Entry Into The Host Human Cell And Its Effect On Human Immune System

The infectious entry of DENV in its target cells, mainly dendritic cells, monocytes, and macrophages, is mediated by the viral envelope glycoprotein E via receptor-mediated endocytosis . The E-protein is the major component (53 kDa) of the virion surface and is arranged as 90 homodimers in mature virions. DENV enters its host cell via clathrin-mediated endocytosis, comparable with other flaviviruses . However, DENV entry via a nonclassical endocytic pathway independent from clathrin has also been described. It seems that the entry pathway chosen by DENV is highly dependent on the cell type and viral strain. In case of the classical endocytic pathway, there is an uptake of the receptor-bound virus by clathrin-coated vesicles. These vesicles fuse with early endosomes to deliver their cargo into the cytoplasm. The Eprotein responds to the reduced pH of the endosome with a large conformational rearrangement. The low pH triggers dissociation of the E-homodimer, which then leads to the insertion of the fusion peptide into the target cell membrane forming a bridge between the virus and the host. Next, a stable trimer of the E-protein is folded into a hairpin-like structure and forces the target membrane to bend towards the viral membrane, and eventually fusion takes place. The fusion results in the release of viral RNA into the cytoplasm for initiation of replication and translation

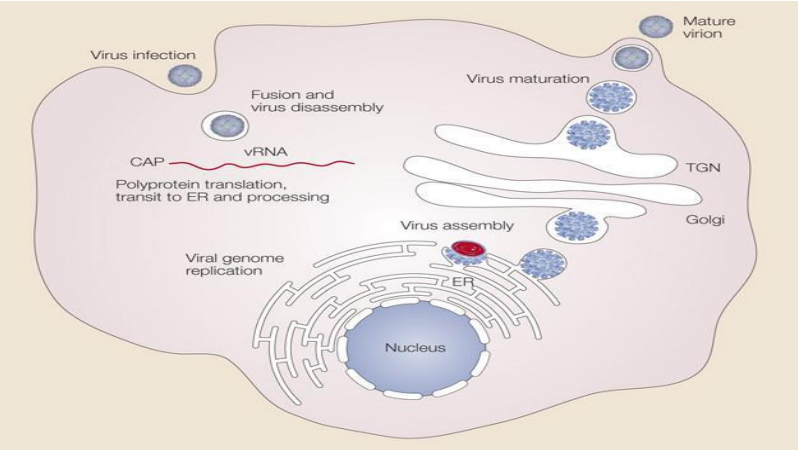


Figure 2: A dengue virus life cycle

Once it is released into the cell cytoplasm, the nucleocapsid opens to uncoat the viral genome. This process releases the viral RNA into the cytoplasm. The viral RNA then hijacks the host cell's machinery to replicate itself. The virus uses ribosomes on the host's rough endoplasmic reticulum (ER) to translate the viral RNA and produce the viral polypeptide. This polypeptide is then cut to form the ten dengue proteins. The newly synthesized viral RNA is enclosed in the C proteins, forming a nucleocapid. The nucleocapsid enters the rough ER and is enveloped in the ER membrane and surrounded by the M and E proteins. This step adds the viral envelope and protective outer layer. The immature viruses travel through the Golgi apparatus complex, where the viruses mature and convert into their infectious form. The mature dengue viruses are then released from the cell and can go on to infect other cells.

As the adaptive immune response starts fighting the dengue infection, B cells produce antibodies called IgM and IgG that are released in the blood and lymph fluid, where they specifically recognize and neutralize the dengue viral particles. In another adaptive immune response, cytotoxic T cells, or killer T cells, recognize and kill the cells that are infected with the dengue virus. The innate immune response activates the complement system, a response that helps the antibodies and white blood cells remove the virus. Together, the innate and adaptive immune responses neutralize the dengue infection, and the patient recovers from dengue fever.

After recovering from a first dengue infection, a person is protected from infection with the remaining three dengue serotypes for two to three months. Unfortunately, it is not long-term protection, and after that short period, a person can be infected with any of the remaining three dengue serotypes.

When a person is infected with a second dengue serotype antibodies from the first infection actually help spread the dengue viral infection and increase viremia, the amount of virus in the bloodstream instead of destroying the virus, the existing antibodies and the antibodies newly produced by the memory B cells can actually help the virus infect host cells more efficiently. Ironically, the consequence of antibody-dependent enhancement is that the body's immune system response actually makes the clinical symptoms of dengue worse and raises the risk of severe dengue illnesses.

during a second infection with dengue, the cytotoxic T cells produced by the immune system provide only partial immunity against the new dengue serotype. The cytotoxic T cells do not effectively clear the virus from the body, and they release excess quantities of molecules called cytokines. In normal quantities, cytokines help the immune response; however, in high quantities, cytokines can produce

serious inflammation and tissue damage such as leakage from the capillaries, possibly contributing to the development of severe dengue diseases.

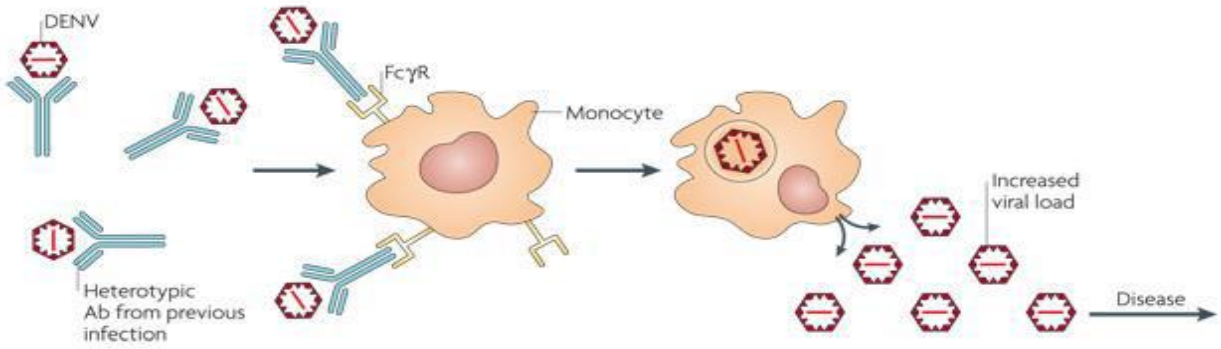


Figure 3: Model of antibody-dependent enhancement of dengue infection

2.2 Strategy For Inhibtion Of Dengue Virus Interaction With The Host Cell

There are four stages of the viral life cycle, and each stage can be considered for the development of drugs. In stage 1, prevent viral entry or infection of the host cell, or inhibit fusion of the viral envelope with the host vesicles. The E protein can be taken as an ideal target. In stage 2, prevent maturation processing of the individual viral protein. The well-studied viral protease is considered a good target. In stage 3, prevent viral RNA synthesis by inhibiting the viral helicase and RdRp. Finally, in stage 4, target the host proteins such as furin and signalase that help the maturation and release of infectious viral particles.

2.3 Human Cell DENV Attachment And Receptors.

Prior to fusion, DENV needs to attach to specific cellular receptors. The virus must interact with a wide variety of cellular receptors.

Inhibiting the DENV entry into host cells can be achieved by inhibiting the DENV receptors present on the cells involved in the fusion process in which the viral genome is injected into the host cell.

Table 1: Different human cell DENV attachment and receptors.

Cell type	Cell description	DENV receptor(s)
Monocytes	Primary myeloid cells	CD14/LPS HSP70/HSP90 Fc-receptor
Dendritic cells	Primary myeloid cells	DC-SIGN
Macrophages	Primary myeloid cells	Mannose receptor CLEC5A
Huh	Hepatocytes	HS
HepG2	Hepatocytes	Laminin receptor, GRP78, HS

2.4 Dendritic Cells (DC-SIGN receptor)

The primary DENV target cells in the skin are believed to be immature dendritic cells (DCs) or Langerhans cells. Immature DCs are very efficient in capturing pathogens whereas mature DCs are relatively resistant to infection. The search for cellular receptors responsible for DENV capture leads to the identification of cell-surface C-type lectin DC-specific intercellular adhesion molecule 3-grabbing nonintegrin (DC-SIGN; CD209. DC-SIGN, mainly expressed by immature DC as a tetramer, is a member of the calcium-dependent C-type lectin family and is composed out of four domains: a cytoplasmic domain responsible for signaling and internalization due to the presence of a

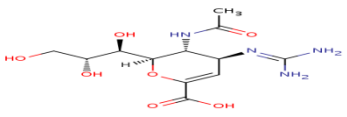
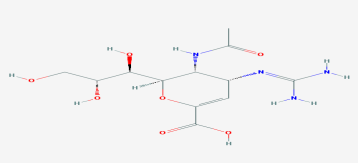
dileucine motif, a transmembrane domain, seven to eight extracellular neck repeats implicated in the oligomerization of DC-SIGN, and a carbohydrate recognition domain (CRD). The CRD recognizes high-mannose N-glycans and fucose-containing blood group antigens. Following antigen capture in the periphery, DCs maturate by upregulation of the costimulatory molecules and migrate to secondary lymphoid organs Activated DCs are stimulators of naive T cells and they initiate production of cytokines and chemokines [85]. Inhibition of the initial interaction between DENV and DC could prevent an immune response. DC-SIGN could be a target for antiviral therapy by interrupting the viral entry process.

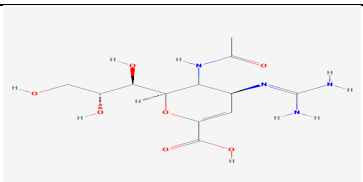
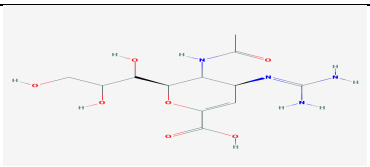
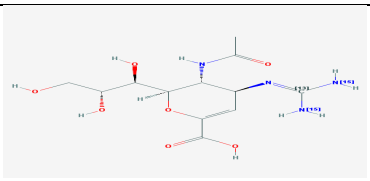
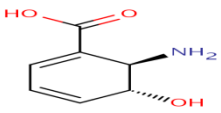
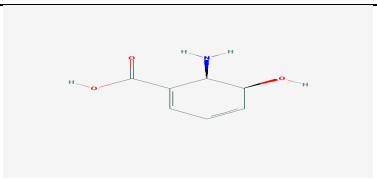
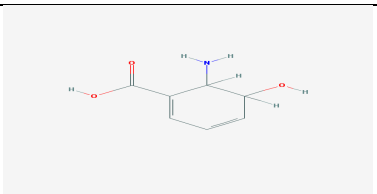
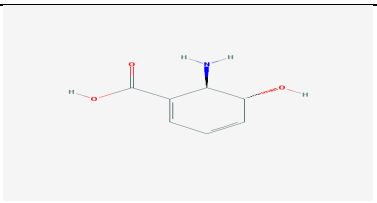
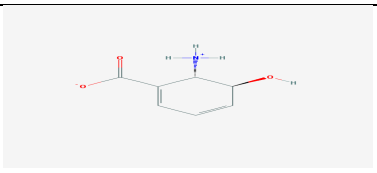
Carbohydrate-binding agents (CBAs) have been shown to prevent capture of DENV to the DC-SIGN receptor on the dendritic cell.

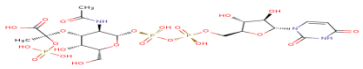
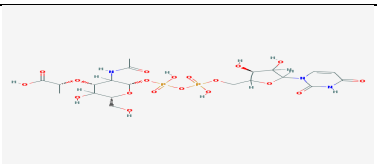
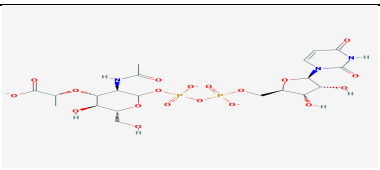
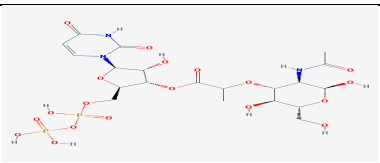
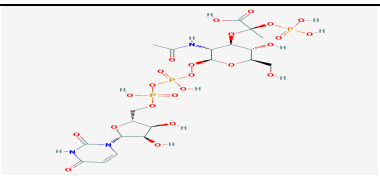
2.5 Potential Ligand Molecules (CBAs).

Hippeastrum hybrid (HHA), *Galanthus nivalis* (GNA), and *Urtica dioica* (UDA), isolated from the amaryllis, snowdrop, and stinging nettle respectively, and their analogues, are the CBAs used as ligands to inhibit the activity of the DC-SIGN receptor during DENV fusion into the dendritic cells.

Table 2: Ligand molecule (CBAs)

Sr. No.	PUBCHEM ID	ALSO KNOWN AS	2D STRUCTURE
1.	CID 60855	Zanamivir (GNA)	
2.	CID 58974096	Talo-zanamivir	

3.	CID 59464423	SureCN12367840	
4.	CID 60076457		
5.	CID 71753010	Zanamir-d3	
6.	CID 448825	Hippeastrum hybrid (HHA)	
7.	CID 17754024	CHEBI:60840	
8.	CID 23422347	CTK0H0810	
9.	CID 46936304	SureCN4317430	
10.	CID 49852385	CPD-9518	

11.	CID 448003	Urtica dioica (UDA)	
12.	CID 25245790		
13.	CID 49852303	UDP-N-acetylmuramate	
14.	CID 53886465		
15.	CID 73350364	CHEMBL2374461	

CHAPTER 3

MATERIALS AND METHODS

3. MATERIALS AND METHODS

3.1 Tools And Softwares

Computational biology and Bioinformatics have the potential to speed up drug discovery processes, reducing the costs of the processes and changing the way the drugs are designed. Rational drug design facilitates and speeds up the drug designing processes that involves various method of identifying novel compounds. One advanced method is the docking of the drug molecule or ligand or inhibitor with the target. The site where the drug binds is known to the site of action, which is responsible for the pharmaceutical effect is the target. Docking is the method by which two molecules bind to each other in 3D space. There are various tools, software and servers meant for docking calculations.

3.1.1 Softwares used are

- Swiss-Pdb Viewer
- Argus Lab 4.0.1
- AutoDockTools-1.5.6rc
- Auto Dock Vina 1.0
- Chimera 1.8.1
- MGL Tools 1.5.6
- Open Babel GUI
- Pymol

3.1.2 Online servers used

- **https://pubchem.ncbi.nlm.nih.gov**
- **http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi?id=index**
- **http://bioserver-3.bioacademy.gr/Bioserver/ChemBioServer/Toxic.php**

3.1.3 Files required for docking

- FASTA sequence of all the CD209 isoforms.
- 3D structure and ".pdb" format file of these isoforms.
- ".sdf" format file of all the inhibitors.
- ".sdf" format file converted to ".pdb" format using Open Babel GUI.
- ".pdbqt" files of both, the proteins as well as the ligand molecules.

3.2 Procedure

- FASTA sequence of all the CD209 isoforms obtained from NCBI.
- 3D structure and ".pdb" format file of these isoforms obtained from PHYRE2.
- In chimera 1.8.1, energy minimization of all the 3D structures of protein molecules was done and saved in ".pdb" format
- ArgusLab 4.0 was used for geometric optimization of these molecules to avoid any error in docking.
- Using AutoDock tools 1.5.6, ".pdb" files of proteins were converted to ".pdbqt" format.
- 3D structures of the ligands were obtained from PubChem. (in ".sdf" format)
- Using Open Babel GUI, ".sdf" format to ".pdb" format
- ".pdb" format of the ligands were converted to ".pdbqt" format using AutoDock tools 1.5.6
- Molecular docking was done using Autodock vina.
- Results from it were saved in ".pdbqt" format
- Results then, were then viewd in PYMOL.
- Toxicity of the results was analyzed in ChemBioserver.

3.3 Methodolgy

Molecular docking is a method which is used for the prediction of preferred orientation of one molecule to other molecule when bound form a stable. It is frequently used to predict the binding energy of small molecular drugs to the targeted protein in order to predict affinity and activity.

3.3.1 Retrieval of amino acid sequences of CD209 protein isoforms from NCBI:

NCBI stands for National Centre for Biotechnological Information. It is established as a division of National Library of Medicines at National Institutes of Health. The NCBI responsible for creating automated systems of knowledge about molecular biology, biochemistry, and genetics, providing the use of such databases and software by the research and medical community; collect biotechnology information both nationally and internationally; and execution research on advanced methods of computer-based information processing for examining the structure and function of biologically important molecules. The URL for this database is http://www.ncbi.nlm.nih.gov.

- The above mentioned URL was browsed.
- In the left search panel "protein" was selected, and in the right search panel "CD209 isoform" was typed and searched.
- FASTA sequence of "CD209 isoform 1", "CD209 isoform 3", "CD209 isoform 4" and "CD209 isoform 5" were obtained and saved in notepad.

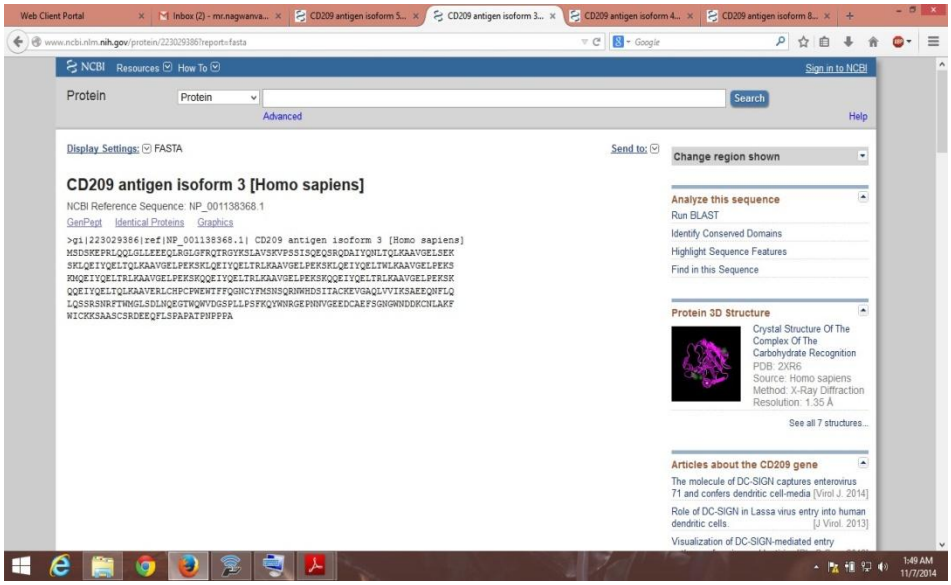


Figure 4: A sample FASTA format sequence

3.3.2 Retrieval of 3D structure of PKM2 Protein modelled by PHYRE2

PHYRE is an automatic fold recognition server for calculating the structure and function of the protein sequence that got submitted in the server. It is used for academic users only. It uses the principle and technique of Homology Modelling and relies on Hidden Markov Models.

- The FASTA sequence, displaying the amino acid sequence, of each of the CD209 isoform was pasted in "amino acid sequence" tab.
- In the "modelling mode" section, "normal" option was checked.
- "Phyre search" was clicked.
- After some time the results were sent to the user given email address.
- The modelled structure was retrieved from the link sent by the server in ".pdb" format.

Figure 5: A view of PHYRE2 website

3.3.3 Energy minimization of all 3D structure of proteins by Chimera 1.8.1:

UCSF CHIMERA 1.7 is an extensible programme for visualization and analysis of molecular structure and related data including density maps, supramolecular associations, sequence alignments, docking results, routes and conformational ensembles. One of the best features is the structural editing job. It can minimize the energy of molecules providing them high stability.

- Chimera window was opened.
- From the option, the 3D structure of protein was retrieved.
- The total resideues were selected.
- From the tool option, by the structure editing option, minimized structure option was clicked.
- The minized structure was saved in ".pdb" format.

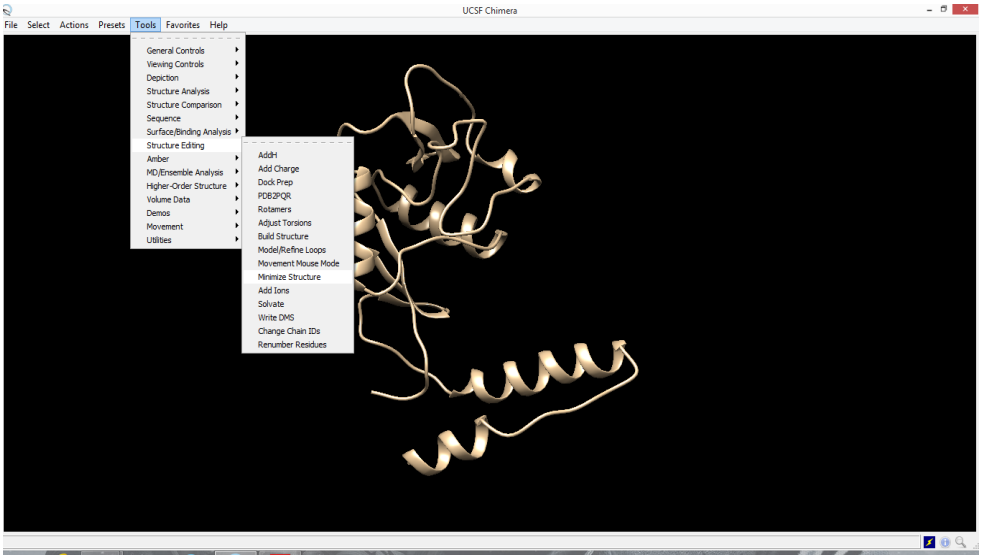


Figure 6: A view of Chimera

3.3.4 Geometry Optimization of all 3D structure of proteins by ArgusLab:

Argus Lab is one of the important software which is used for the geometry optimization of the Protein molecule which we need to dock. This is done because when we dock with the ligand molecules it gives a perfect result without any errors. It optimize the geometry of the molecule for better orientation

- ArgusLab 4.0 window was opened
- From the option file, the 3D structure of protein was retrieved
- Then go to geometry optimization tools
- From the tool option, by the structure editing option, Optimize geometry option was clicked.
- The Optimized structure was saved in .pdb format

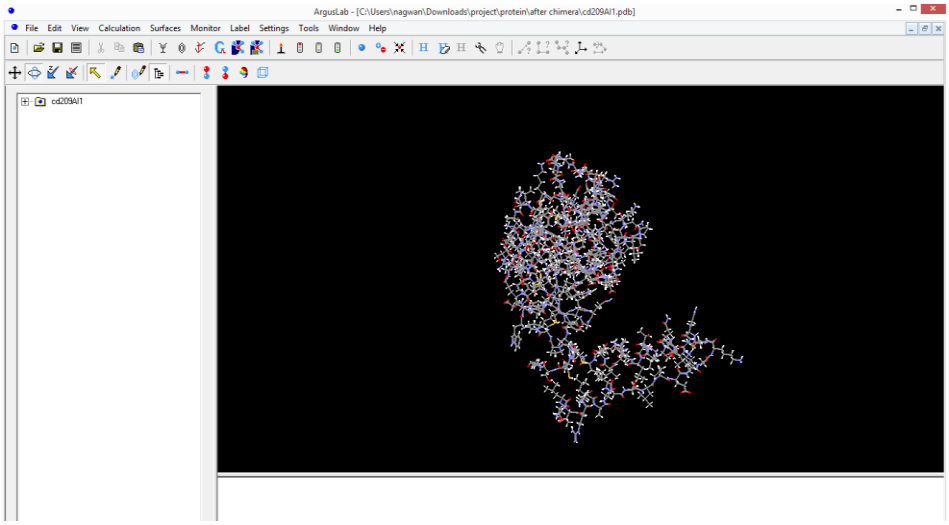


Figure 7: A view of ArgusLab

3.3.5 Collect SDF files of CD209 Inhibitor molecules from PubChem:

PubChem is a database of chemical structures of small organic molecules and contain information of their biological activity, origin and related literatures. It is executed and updated by NCBI and is freely available. Millions of compound structures and data seta can be freely downloaded in ".sdf" format.

- PubChem page was retrieved by browsing Pubchem.ncbi.nlm.nih.gov
- In search bar individual inhibitors name was typed and entered
- All the available ligands of therapeutic target database retrieved in ".sdf" file format

3.3.6 Conversion of .sdf file format to .pdb by Open Babel GUI:

Open Babel 2.3.1 is a chemical toolkit designed to interpret the various language of chemical data. It allows searching, converting, and analyzing chemical data. It supports Cheminformatics, molecular modelling, and bioinformatics. It coverts chemical data from one file format to another.

- Open Babel 2.3.1 window was opened
- The input format was selected as ".sdf" and the output format as ".pdb".
- From the input option ".sdf" file was browsed.
- Click on the convert option to convert ".sdf" file format to ".pdb" file format.
- Then the selected files were generated in the ".pdb" file format and saved.

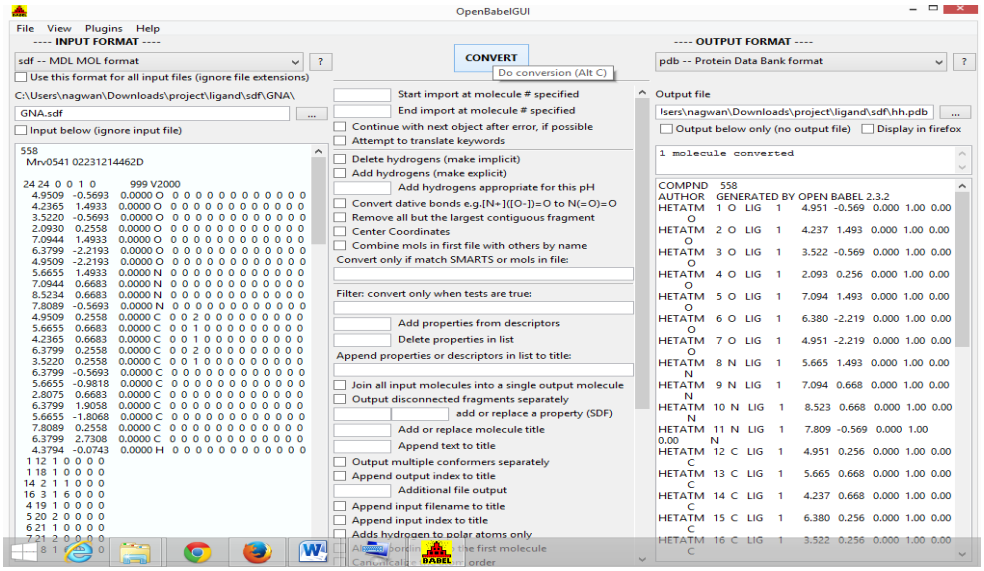


Figure 8: A view of OpenBabel GUI

3.3.7 Conversion of .pdb to .pdbqt of Molecules Using Auto Dock Tools 1.5.6:

Auto Dock 4.0 is an Interactive Molecular graphics program developed by The Scripps Research Institute for estimating docking calculations and displaying docking modes of pairs of protein and ligand molecules. Auto Dock is used as the docking tool which calculates intermolecular "energies" by adding up all intermolecular interactions, adding polar hydrogens and also the kollmann charges to the protein molecule (e.g. van der Waals, electrostatic) that occur between a ligand and protein target.

- Then we open the ".pdb" file in Autodock tools (version 1.5.6) software.
- We add hydrogen to the molecule (polar only).

- Go to grid ⟶ macromolecule ⟶ choose ⟶ save as "**.pdbqt"** file
- Click on grid again and then click on grid box.
- Then we set the desired values in grid box .
- Next for the ligand we click on ligand ⟶ input ⟶ open ⟶ open the inhibitors ".pdb" file.
- Go to ligand ⟶ torsion tree ⟶ choose torsions ⟶ done.
- Click ligand ⟶ torsion tree ⟶ detect root.
- Save the file by ligand ⟶ output ⟶ save as "**.pdbqt"**.

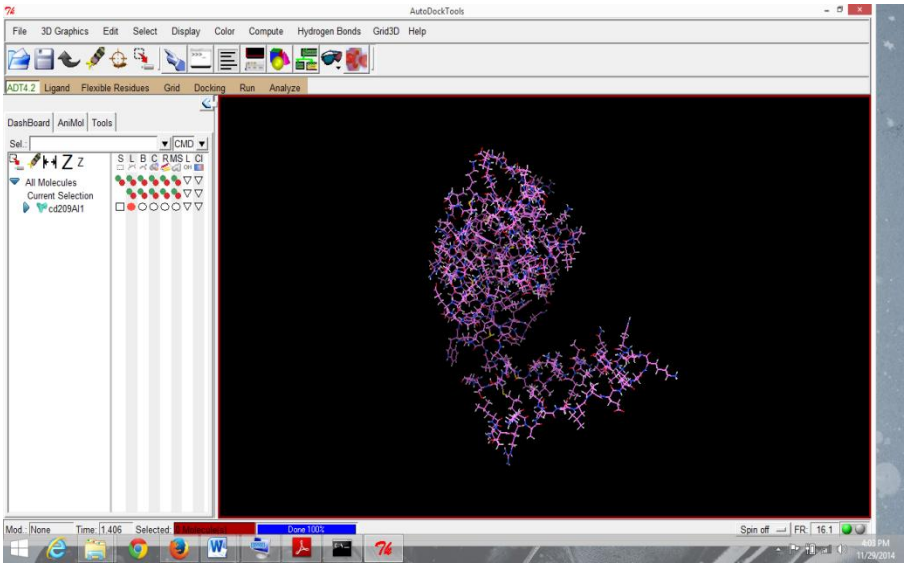


Figure 9: Autodock tools (version 1.5.6) software

3.3.8 Molecular Docking Using Auto DockVina:

AutoDock Vina significantly improves the average accuracy of the binding mode predictions compared to AutoDock 1.5.6, judging by various tests according to The Scripps Research Institute the training set used in AutoDock 1.5.6 development. Additionally and independently, AutoDock Vina has been tested against a virtual screening benchmark called the Directory of Useful Decoys.

- Create a conf.txt file giving the information of configuration for the Docking process in the same folder where we have the protein and its inhibitor in the ".pdbqt" format.

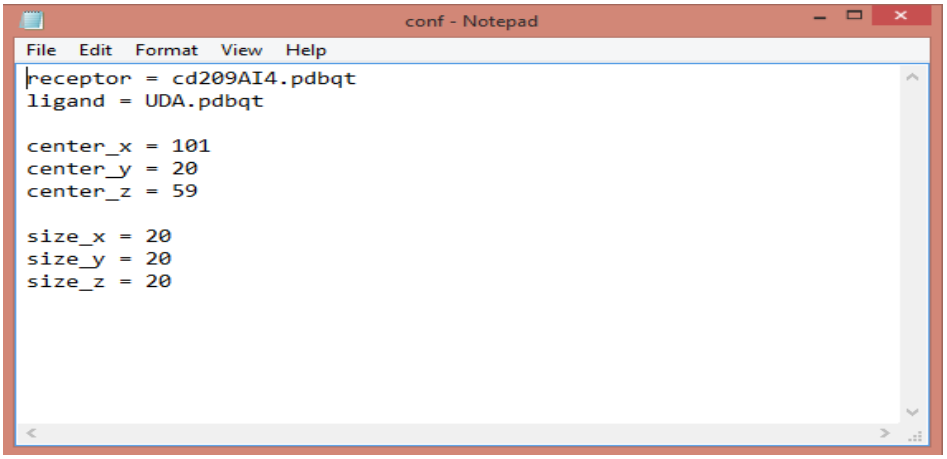


Figure 10: A sample conf.txt file

- Open the Command prompt in the system.
- Give the location where the ".pdbqt" files of both Protein and inhibitor in cmd.
- Then give the location of program vina in the program file for processing.
- Give the command in the cmd for docking procedure to initiate.
- Result is displayed in the log file generated by the AutoDock Vina.

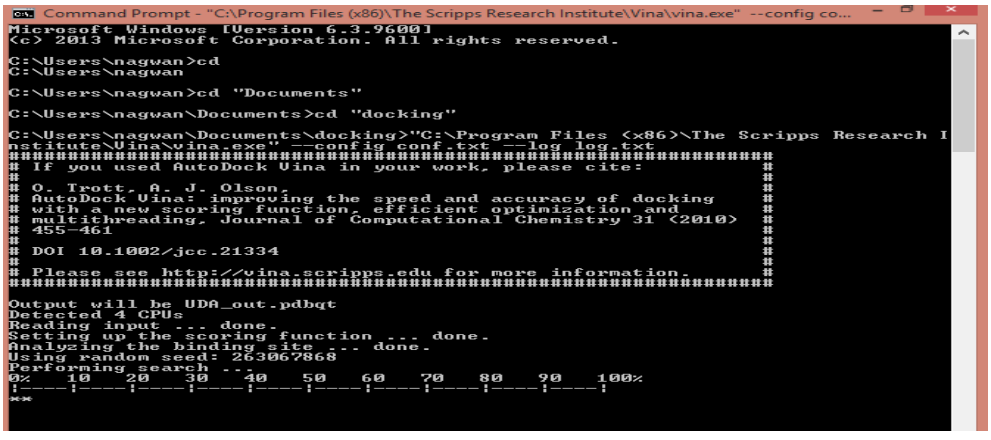


Figure 11: Docking process in cmd

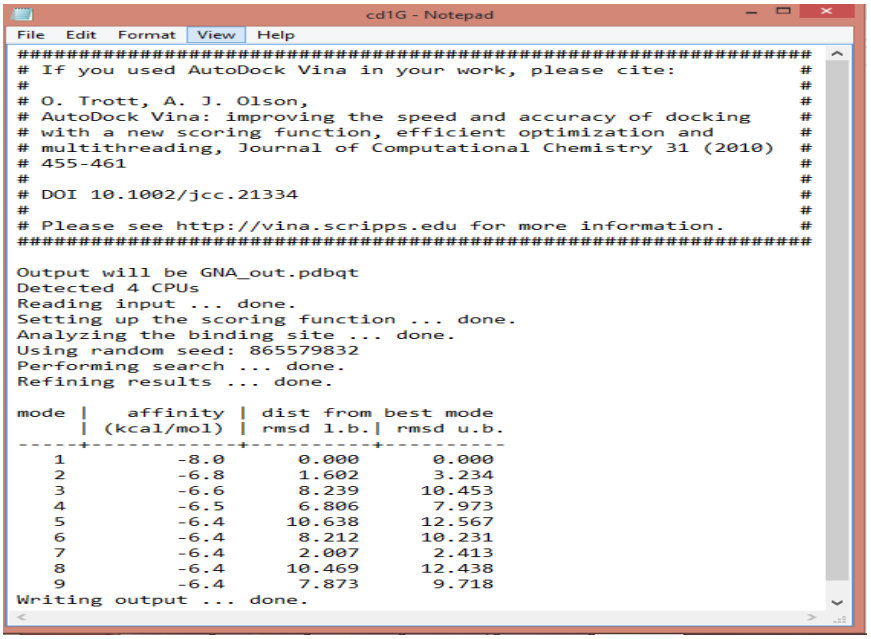


Figure 12: Docking result as log.txt file

3.3.9 Toxicity Prediction by Chem Bio server:

This is a Server which is part of the Bio academy **Bio server** that contains some tools and web services developed in the Biomedical Research Foundation of the Academy of Athens. Its main aim is to improve computational molecule screening and analysis and it is financed by the Greek Ministry of Education Cooperation Proposal Entitled as PIK3CA Oncogenic Mutations in Breast and Colon Cancers.

a) The ligand molecule in either ".mol" or ".sdf" format is uploaded

b) Then on clicking "Process Data" at the end of the page, it gives the result whether the compound is toxic or nontoxic.

c) If the compound is toxic, it shows because of which molecule.

CHAPTER 4

RESULTS

4. RESULTS

4.1 3d Structures Of CD209 Antigen Isoforms Obtained From Phyre2.

The Phyre2 servers predict the three-dimensional structure of a protein sequence using the principles and techniques of homology modeling. Following 3D structures of CD209 Isoforms were obtained from it:

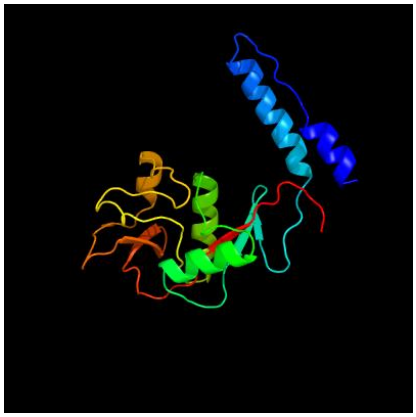


Figure 13: CD209 Isoform 1

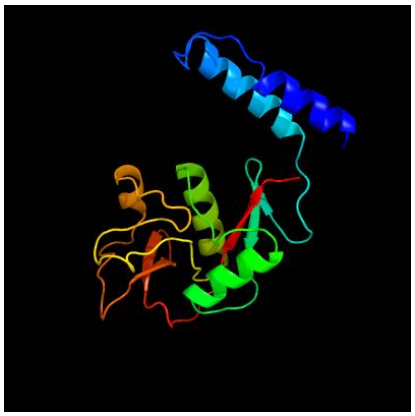


Figure 14: CD209 Isoform 3

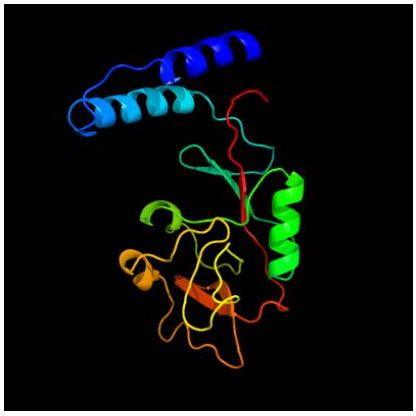


Figure 15: CD209 Isoform 4

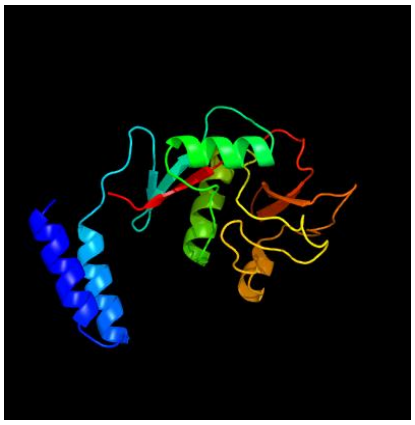


Figure 16: CD209 Isoform 5

4.2 Docking Results Of CD209 Isoforms With All The Inhibitors

CD209 isoform 1, CD209 isoform 3, CD209 isoform 4 and CD209 isoform 5 were docked with all the inhibitors and the results were saved in ".txt" and ".pdbqt" format respectively, for further use.

- First we use ".pdbqt" format of the results and visualize them in PYMOL.
- Usinf ".txt" file , we analyze the affinity of the inhibitors with the protein site.

4.2.1 Results of docking Inhibitors with CD209 Isoform 1 in AUTODOCK Vina:

```
Output will be GNA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 865579832
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -8.0      0.000      0.000
   2        -6.8      1.602      3.234
   3        -6.6      8.239     10.453
   4        -6.5      6.806      7.973
   5        -6.4     10.638     12.567
   6        -6.4      8.212     10.231
   7        -6.4      2.007      2.413
   8        -6.4     10.469     12.438
   9        -6.4      7.873      9.718
Writing output ... done.
```

Table 3: CID 60855

```
Output will be GNA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2138149080
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.9      0.000      0.000
   2        -5.8      7.033      8.618
   3        -5.7      5.137      7.159
   4        -5.6      8.491     10.248
   5        -5.6      7.475      9.076
   6        -5.6      7.464      8.930
   7        -5.6      5.265      7.435
   8        -5.5      8.382     10.725
   9        -5.3      8.924     10.422
Writing output ... done.
```

Table 4: CID 58974096

```
Output will be GNA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1231732640
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.8      0.000      0.000
   2        -5.8      7.125      8.704
   3        -5.7      1.632      3.769
   4        -5.7      5.211      7.242
   5        -5.6      8.573     10.328
   6        -5.6      7.578      9.187
   7        -5.6      7.556      9.004
   8        -5.5      5.328      7.510
   9        -5.4      8.454     10.802
Writing output ... done.
```

Table 5: CID 59464423

```
Output will be GNA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 111279156
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.5      0.000      0.000
   2        -5.5      2.795      4.121
   3        -5.5      3.425      4.889
   4        -5.5      2.237      4.354
   5        -5.5      2.869      4.124
   6        -5.4      1.602      3.669
   7        -5.3      3.217      5.030
   8        -5.3      5.129      7.016
   9        -5.3      3.356      5.097
Writing output ... done.
```

Table 6: CID 60076457

```
Output will be GNA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1216270448
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.6      0.000      0.000
   2        -5.6      2.765      4.084
   3        -5.5      2.291      3.369
   4        -5.5      1.368      3.561
   5        -5.4      2.543      3.249
   6        -5.4      2.124      3.406
   7        -5.3      2.429      4.131
   8        -5.2      2.250      4.308
   9        -5.2      3.879      5.875
Writing output ... done.
```

Table 7: CID 71753010

```
Output will be HHA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1767568960
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -4.1      0.000      0.000
   2        -4.1      2.164      3.882
   3        -3.8     11.725     13.130
   4        -3.7      7.291      7.886
   5        -3.7      1.129      3.688
   6        -3.7      5.867      7.172
   7        -3.6      9.032     10.402
   8        -3.5      9.047     11.116
   9        -3.5      7.521      9.025
Writing output ... done.
```

Table 8: CID 448825

```
Output will be HHA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 927889344
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.0      0.000      0.000
   2        -4.8      1.272      1.661
   3        -4.6      1.229      1.441
   4        -4.5      1.909      2.529
   5        -4.4      1.930      2.798
   6        -4.2      8.519      9.021
   7        -4.1     12.781     13.796
   8        -4.1      9.606     10.454
   9        -4.0     12.114     13.184
Writing output ... done.
```

Table 9: CID 17754024

```
Output will be HHA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1367163872
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.0      0.000      0.000
   2        -4.8      1.264      1.658
   3        -4.3      1.769      2.246
   4        -4.2      8.433      8.963
   5        -4.1     12.755     13.768
   6        -4.1      1.735      2.610
   7        -4.1      9.574     10.420
   8        -4.0      8.259      8.675
   9        -4.0      8.362      9.073
Writing output ... done.
```

Table 10: CID 23422347

Output will be HHA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1727099400
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-5.0	0.000	0.000
2	-4.8	1.264	1.658
3	-4.6	1.763	2.391
4	-4.5	1.312	2.748
5	-4.2	8.367	8.946
6	-4.1	12.764	13.775
7	-4.1	1.473	2.307
8	-4.1	9.583	10.427
9	-3.9	1.678	2.301

Writing output ... done.

Table 11: CID 46936304

Output will be HHA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -436015968
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-5.0	0.000	0.000
2	-5.0	1.259	1.656
3	-4.9	1.770	2.338
4	-4.7	1.676	2.877
5	-4.3	8.655	9.072
6	-4.3	12.754	13.799
7	-4.1	1.610	1.974
8	-4.0	9.738	10.696
9	-4.0	8.248	9.083

Writing output ... done.

Table 12: CID 49852385

Output will be UDA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1090229528
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-12.4	0.000	0.000
2	-12.1	1.441	2.015
3	-11.7	2.142	7.774
4	-11.7	2.556	8.033
5	-11.7	2.251	2.851
6	-11.6	4.690	7.067
7	-11.5	2.876	8.066
8	-11.5	3.758	5.393
9	-11.4	1.447	7.910

Writing output ... done.

Table 13: CID 448003

Output will be UDA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1196378296
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-8.2	0.000	0.000
2	-8.1	1.326	1.552
3	-7.8	2.788	3.323
4	-7.6	1.798	2.225
5	-7.1	2.084	9.110
6	-7.0	1.592	1.950
7	-7.0	2.383	4.207
8	-6.8	2.705	9.033
9	-6.7	2.934	9.694

Writing output ... done.

Table 14: CID 49852303

Output will be UDA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1330190464
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-9.9	0.000	0.000
2	-9.7	0.876	2.125
3	-9.1	1.676	2.850
4	-8.7	1.970	8.524
5	-8.6	2.362	9.190
6	-8.4	2.105	3.357
7	-8.3	1.862	2.416
8	-8.2	3.295	4.876
9	-8.0	3.628	9.797

Writing output ... done.

Table 15: CID 53886465

Output will be UDA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1200455040
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-7.6	0.000	0.000
2	-7.3	2.597	6.666
3	-7.3	3.380	8.255
4	-7.2	3.691	6.134
5	-7.2	2.568	6.801
6	-7.2	2.292	4.370
7	-7.2	2.534	6.622
8	-7.1	2.306	4.596
9	-7.1	3.244	5.647

Writing output ... done.

Table 16: CID 73350364

Output will be UDA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -383233516
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-9.8	0.000	0.000
2	-9.3	1.767	2.261
3	-8.9	0.868	1.595
4	-8.0	1.935	2.620
5	-7.9	2.578	10.270
6	-7.3	2.459	9.988
7	-7.2	2.954	10.448

Writing output ... done.

Table 17: CID 25245790

4.2.2 Results of docking Inhibitors with CD209 Isoform 3 in AUTODOCK Vina:

Output will be GNA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1677299108
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-7.8	0.000	0.000
2	-7.4	5.969	7.545
3	-7.4	5.341	6.716
4	-7.3	5.079	6.816
5	-7.1	5.259	6.924
6	-7.1	7.172	9.422
7	-7.0	4.912	6.686
8	-7.0	1.577	3.215
9	-7.0	5.713	7.235

Writing output ... done.

Table 18: CID 60855

Output will be GNA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1795766632
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.2	0.000	0.000
2	-6.1	1.741	2.319
3	-6.0	2.012	4.054
4	-5.9	2.453	4.617
5	-5.8	2.623	4.488
6	-5.7	2.173	5.434
7	-5.7	1.943	3.605
8	-5.7	2.873	5.197
9	-5.4	3.080	5.415

Writing output ... done.

Table 19: CID 58974096

Output will be GNA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -794880008
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.2	0.000	0.000
2	-6.1	1.745	2.333
3	-6.0	2.008	4.037
4	-5.9	2.452	4.603
5	-5.8	2.616	4.462
6	-5.8	1.271	3.167
7	-5.7	6.491	9.110
8	-5.7	2.539	4.976
9	-5.6	2.070	5.356

Writing output ... done.

Table 20: CID 59464423

Output will be GNA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -883720624
Performing search ... done.
Refining results ... done.

mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-6.2	0.000	0.000
2	-6.1	1.764	2.362
3	-5.9	2.027	4.052
4	-5.9	7.617	9.856
5	-5.9	2.485	4.638
6	-5.9	6.866	9.397
7	-5.8	2.634	4.486
8	-5.7	2.477	4.938
9	-5.7	1.835	4.898

Writing output ... done.

Table 21: CID 60076457

```
Output will be GNA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1872870864
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -6.2      0.000      0.000
   2        -6.1      1.745      2.320
   3        -5.9      1.281      3.166
   4        -5.9      2.009      4.034
   5        -5.9      2.451      4.618
   6        -5.8      2.639      4.474
   7        -5.6      2.036      5.329
   8        -5.5      2.172      4.268
   9        -5.4      2.318      4.539
Writing output ... done.
```

Table 22: CID 71753010

```
Output will be HHA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 960165804
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -4.7      0.000      0.000
   2        -4.5      1.744      3.304
   3        -4.3      1.878      2.287
   4        -4.2      1.834      2.222
   5        -4.0      1.745      3.632
   6        -3.9      2.400      2.774
   7        -3.8      7.210      8.299
   8        -3.7      2.522      3.964
   9        -3.7      7.006      8.024
Writing output ... done.
```

Table 23: CID 448825

```
Output will be HHA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -181186592
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.0      7.781      8.633
   3        -4.9      1.571      2.509
   4        -4.8      1.482      1.803
   5        -4.7      7.794      8.604
   6        -4.6      0.699      1.055
   7        -4.5      6.957      7.760
   8        -4.4      3.117      3.931
   9        -4.2      1.631      3.037
Writing output ... done.
```

Table 24: CID 17754024

```
Output will be HHA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -501937024
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.0      7.762      8.618
   3        -4.9      1.581      2.500
   4        -4.8      1.479      1.803
   5        -4.6      7.203      7.781
   6        -4.5      7.062      7.830
   7        -4.4      2.082      2.948
   8        -4.4      8.305      8.734
   9        -4.3      3.003      3.834
Writing output ... done.
```

Table 25: CID 23422347

```
Output will be HHA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -178701324
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.0      7.768      8.620
   3        -4.9      1.553      2.505
   4        -4.8      1.548      1.869
   5        -4.8      7.840      8.666
   6        -4.4      2.080      2.937
   7        -4.4      3.129      3.948
   8        -4.2      1.649      3.053
   9        -4.2      7.083      7.913
Writing output ... done.
```

Table 26: CID 46936304

```
Output will be HHA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1626925056
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.1      7.734      8.634
   3        -5.0      8.263      8.833
   4        -4.9      7.655      8.451
   5        -4.4      7.296      8.027
   6        -4.3      9.108     10.062
   7        -4.2      7.920      8.896
   8        -4.1      8.044      8.736
   9        -4.1      9.270     10.229
Writing output ... done.
```

Table 27: CID 49852385

```
Output will be UDA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1662853056
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1       -13.2      0.000      0.000
   2       -13.1      1.295      2.376
   3       -12.4      2.122      7.631
   4       -12.4      1.591      7.566
   5       -12.4      1.379      2.448
   6       -12.1      3.257      8.683
   7       -12.0      4.260      9.043
   8       -11.7      1.888      2.383
   9       -11.7      1.578      7.109
Writing output ... done.
```

Table 28: CID 448003

```
Output will be UDA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1388162320
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -8.3      0.000      0.000
   2        -8.3      1.106      1.226
   3        -8.0      1.696      2.297
   4        -7.9      1.102      1.320
   5        -7.6      1.953      3.117
   6        -7.6      3.826      4.335
   7        -7.4      3.178      9.245
   8        -6.9      3.224     10.069
   9        -6.4      1.882      3.023
Writing output ... done.
```

Table 29: CID 49852303

```
Output will be UDA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1900795224
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -9.5      0.000      0.000
   2        -9.1      1.138      2.351
   3        -8.8      1.857      3.173
   4        -8.8      1.652      2.175
   5        -8.1      2.132      8.943
   6        -7.9      2.249      2.892
   7        -7.7      3.251      9.526
   8        -7.5      1.742      2.734
   9        -7.5      1.933      2.164
Writing output ... done.
```

Table 30: CID 53886465

```
Output will be UDA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 247656760
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -8.1      0.000      0.000
   2        -7.9      2.696      5.099
   3        -7.9      1.058      2.076
   4        -7.7      2.731      4.688
   5        -7.6      2.619      6.794
   6        -7.6      3.096      7.180
   7        -7.5      3.291      7.519
   8        -7.3      2.798      7.312
   9        -7.3      3.196      7.480
Writing output ... done.
```

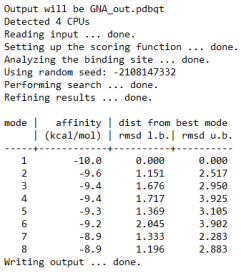
Table 31: CID 73350364

```
Output will be UDA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2059832484
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -9.6      0.000      0.000
   2        -9.5      1.843      2.605
   3        -9.5      2.093      2.660
   4        -9.4      1.088      1.589
   5        -8.8      2.540      9.927
   6        -8.4      1.914      3.095
   7        -8.4      2.848     10.229
   8        -8.4      1.684      2.273
   9        -8.1      2.985     10.128
Writing output ... done.
```

Table 32: CID 25245790

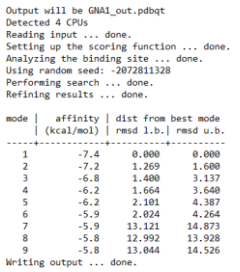
4.2.3 Results of docking Inhibitors with CD209 Isoform 4 in AUTODOCK Vina:



```
Output will be GNA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2108147332
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -10.0      0.000      0.000
   2         -9.6      1.151      2.517
   3         -9.4      1.676      2.950
   4         -9.4      1.717      3.925
   5         -9.3      1.369      3.105
   6         -9.2      2.045      3.902
   7         -8.9      1.333      2.283
   8         -8.9      1.196      2.883
Writing output ... done.
```

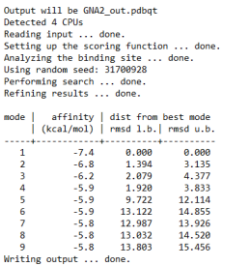
Table 33: CID 60855



```
Output will be GNA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -2072811328
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.4      0.000      0.000
   2         -7.2      1.269      1.600
   3         -6.8      1.400      3.137
   4         -6.2      1.664      3.640
   5         -6.2      2.101      4.387
   6         -5.9      2.024      4.264
   7         -5.9     13.121     14.873
   8         -5.8     12.992     13.928
   9         -5.8     13.044     14.526
Writing output ... done.
```

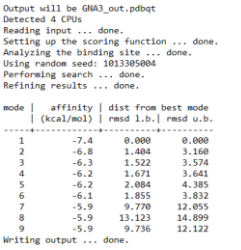
Table 34: CID 58974096



```
Output will be GNA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 31700928
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.4      0.000      0.000
   2         -6.8      1.394      3.135
   3         -6.2      2.079      4.377
   4         -5.9      1.920      3.833
   5         -5.9      9.722     12.114
   6         -5.9     13.122     14.855
   7         -5.8     12.987     13.926
   8         -5.8     13.032     14.520
   9         -5.8     13.803     15.456
Writing output ... done.
```

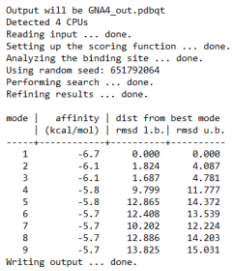
Table 35: CID 59464423



```
Output will be GNA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1013305004
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -7.4      0.000      0.000
   2         -6.8      1.404      3.160
   3         -6.3      1.522      3.574
   4         -6.2      1.671      3.641
   5         -6.2      2.084      4.385
   6         -6.1      1.855      3.832
   7         -5.9      9.770     12.055
   8         -5.9     13.123     14.899
   9         -5.9      9.736     12.122
Writing output ... done.
```

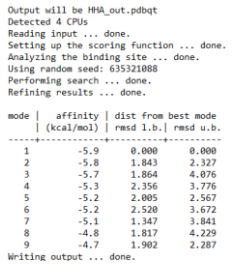
Table 36: CID 60076457



```
Output will be GNA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 651792064
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -6.7      0.000      0.000
   2         -6.1      1.824      4.087
   3         -6.1      1.687      4.781
   4         -5.8      9.799     11.777
   5         -5.8     12.865     14.372
   6         -5.7     12.408     13.539
   7         -5.7     10.202     12.224
   8         -5.7     12.886     14.203
   9         -5.7     13.825     15.031
Writing output ... done.
```

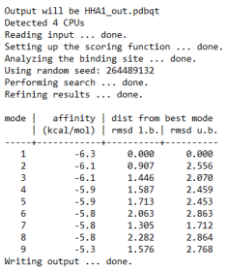
Table 37: CID 71753010



```
Output will be HHA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 635321088
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -5.9      0.000      0.000
   2         -5.8      1.843      2.327
   3         -5.7      1.864      4.076
   4         -5.3      2.356      3.776
   5         -5.2      2.005      2.567
   6         -5.2      2.520      3.672
   7         -5.1      1.347      3.841
   8         -4.8      1.817      4.229
   9         -4.7      1.902      2.287
Writing output ... done.
```

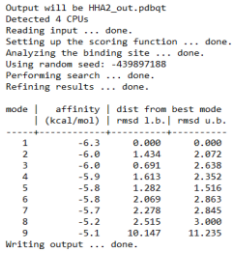
Table 38: CID 448825



```
Output will be HHA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 264489132
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -6.3      0.000      0.000
   2         -6.1      0.907      2.556
   3         -6.1      1.446      2.070
   4         -5.9      1.587      2.459
   5         -5.9      1.713      2.453
   6         -5.8      2.063      2.863
   7         -5.8      1.305      1.712
   8         -5.8      2.282      2.864
   9         -5.3      1.576      2.768
Writing output ... done.
```

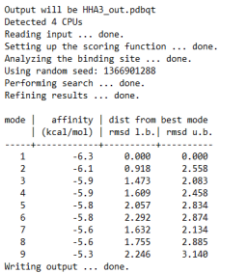
Table 39: CID 17754024



```
Output will be HHA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -439897188
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -6.3      0.000      0.000
   2         -6.0      1.434      2.072
   3         -6.0      0.691      2.638
   4         -5.9      1.613      2.352
   5         -5.8      1.282      1.516
   6         -5.8      2.069      2.863
   7         -5.7      2.278      2.845
   8         -5.2      2.515      3.000
   9         -5.1     10.147     11.235
Writing output ... done.
```

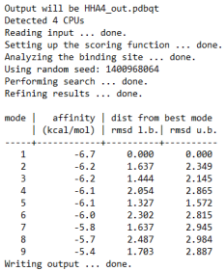
Table 40: CID 23422347



```
Output will be HHA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1366901288
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -6.3      0.000      0.000
   2         -6.1      0.918      2.558
   3         -5.9      1.473      2.083
   4         -5.9      1.609      2.458
   5         -5.8      2.057      2.834
   6         -5.8      2.292      2.874
   7         -5.6      1.632      2.134
   8         -5.6      1.755      2.885
   9         -5.3      2.246      3.140
Writing output ... done.
```

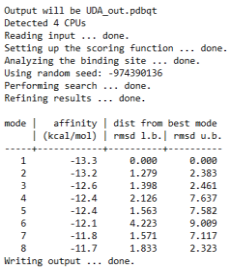
Table 41: CID 46936304



```
Output will be HHA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1400968064
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1         -6.7      0.000      0.000
   2         -6.2      1.637      2.349
   3         -6.2      1.444      2.145
   4         -6.1      2.054      2.865
   5         -6.1      1.327      1.572
   6         -6.0      2.302      2.815
   7         -5.8      1.637      2.945
   8         -5.7      2.487      2.984
   9         -5.4      1.703      2.887
Writing output ... done.
```

Table 42: CID 49852385



```
Output will be UDA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -974390136
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -13.3      0.000      0.000
   2        -13.2      1.279      2.383
   3        -12.6      1.398      2.461
   4        -12.4      2.126      7.637
   5        -12.4      1.563      7.582
   6        -12.1      4.223      9.009
   7        -11.8      1.571      7.117
   8        -11.7      1.833      2.323
Writing output ... done.
```

Table 43: CID 448003

4.2.4 Results of docking Inhibitors with CD209 Isoform 5 in AUTODOCK Vina

```
Output will be GNA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -887881792
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -7.8      0.000      0.000
   2        -7.4      5.333      6.716
   3        -7.3      5.091      6.821
   4        -7.3      6.254      8.086
   5        -7.1      5.304      6.941
   6        -7.1      5.902      7.338
   7        -7.0      6.589      7.487
   8        -7.0      4.935      6.706
   9        -7.0      4.948      6.447
Writing output ... done.
```

Table 44: CID 60855

```
Output will be GNA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1978162801
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -6.3      0.000      0.000
   2        -6.3      1.696      2.231
   3        -6.0      1.981      4.023
   4        -5.9      2.400      4.580
   5        -5.9      2.623      4.456
   6        -5.8      2.412      4.907
   7        -5.8      2.078      5.400
   8        -5.5      2.123      4.241
   9        -5.4      3.108      5.461
Writing output ... done.
```

Table 45: CID 58974096

```
Output will be GNA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 2077438128
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -6.3      0.000      0.000
   2        -6.3      1.719      2.282
   3        -6.1      0.990      3.174
   4        -6.0      6.038      8.037
   5        -6.0      1.835      3.683
   6        -6.0      1.526      3.329
   7        -6.0      1.623      3.568
   8        -6.0      1.596      3.814
   9        -5.9      1.736      4.024
Writing output ... done.
```

Table 46: CID 59464423

```
Output will be GNA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 558037184
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -6.3      0.000      0.000
   2        -6.3      1.742      2.331
   3        -6.1      0.992      3.172
   4        -6.0      1.526      3.328
   5        -6.0      1.617      3.567
   6        -5.9      1.763      4.839
   7        -5.9      1.593      3.804
   8        -5.8      1.734      4.062
   9        -5.5      2.184      4.231
Writing output ... done.
```

Table 47: CID 60076457

```
Output will be GNA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 65095564
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -6.3      0.000      0.000
   2        -6.2      1.703      2.248
   3        -6.0      1.986      4.021
   4        -5.9      2.407      4.599
   5        -5.8      2.700      4.481
   6        -5.8      2.504      4.916
   7        -5.8      2.091      5.420
   8        -5.7      2.849      5.089
   9        -5.5      2.191      4.252
Writing output ... done.
```

Table 48: CID 71753010

```
Output will be HHA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 1189971000
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -4.8      0.000      0.000
   2        -4.5      1.752      3.313
   3        -4.2      1.815      2.215
   4        -4.2      7.415      8.641
   5        -4.1      2.165      2.975
   6        -4.1      2.291      4.082
   7        -4.0      1.894      2.118
   8        -3.9      2.114      2.616
   9        -3.8      2.441      3.513
Writing output ... done.
```

Table 49: CID 448825

```
Output will be HHA1_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -1990036528
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.0      7.801      8.662
   3        -4.9      1.572      2.499
   4        -4.8      1.482      1.807
   5        -4.6      0.915      2.626
   6        -4.5      7.067      7.838
   7        -4.4      3.176      3.981
   8        -4.3      7.456      8.064
   9        -4.2      1.758      3.014
Writing output ... done.
```

Table 50: CID 17754024

```
Output will be HHA2_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -83517472
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -4.9      1.575      2.494
   3        -4.8      1.485      1.808
   4        -4.6      7.214      7.803
   5        -4.4      2.085      2.962
   6        -4.3      2.996      3.825
   7        -4.1      1.675      2.111
   8        -4.1      2.059      3.215
   9        -4.0      8.203      8.669
Writing output ... done.
```

Table 51: CID 23422347

```
Output will be HHA3_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -996926232
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.0      7.791      8.656
   3        -4.9      1.576      2.498
   4        -4.8      1.466      1.792
   5        -4.5      7.525      8.342
   6        -4.5      7.065      7.845
   7        -4.4      2.053      2.946
   8        -4.4      1.836      2.235
   9        -4.3      2.992      3.819
Writing output ... done.
```

Table 52: CID 46936304

```
Output will be HHA4_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: 180753872
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1        -5.2      0.000      0.000
   2        -5.1      7.785      8.669
   3        -5.1      8.288      8.892
   4        -4.9      7.695      8.516
   5        -4.6      7.367      8.017
   6        -4.4      7.310      8.301
   7        -4.3      9.118     10.071
   8        -4.3      7.734      8.372
   9        -4.1      8.697      9.403
Writing output ... done.
```

Table 53: CID 49852385

```
Output will be UDA_out.pdbqt
Detected 4 CPUs
Reading input ... done.
Setting up the scoring function ... done.
Analyzing the binding site ... done.
Using random seed: -974390136
Performing search ... done.
Refining results ... done.

mode |   affinity | dist from best mode
     | (kcal/mol) | rmsd l.b.| rmsd u.b.
-----+------------+----------+----------
   1       -13.3      0.000      0.000
   2       -13.2      1.279      2.383
   3       -12.6      1.398      2.461
   4       -12.4      2.126      7.637
   5       -12.4      1.563      7.582
   6       -12.1      4.223      9.009
   7       -11.8      1.571      7.117
   8       -11.7      1.833      2.323
Writing output ... done.
```

Table 54: CID 448003

4.3 Summary Of All The Docking Results From Autodock Vina

Table 55: Summary Of All The Docking Results From Autodock Vina

Sr. No.	Ligand		Receptor			
	PubChem ID	Also known as	CD209 antigen isoforms [Homo sapiens] (Binding energy in kcal/mol)			
			1	3	4	5
1.	CID 60855	Zanamivir	-8.0	-7.8	-10.0	-7.8
2.	CID 58974096	Talo-zanamivir	-5.9	-6.9	-7.4	-6.3
3.	CID 59464423	SureCN12367840	-5.8	-6.0	-7.3	-6.3
4.	CID 60076457		-5.5	-6.2	-7.6	-6.2
5.	CID 71753010	Zanamir-d3	-5.6	-6.3	-6.7	-6.0
6.	CID 448825	HHA	-4.1	-4.7	-5.9	-4.8
7.	CID 17754024	CHEBI:60840	-5.0	-5.2	-6.1	-5.2
8.	CID 23422347	CTK0H0810	-5.0	-5.1	-6.2	-5.2
9.	CID 46936304	SureCN4317430	-4.8	-5.2	-6.3	-5.1
10.	CID 49852385	CPD-9518	-4.7	-5.1	-6.2	-5.2
11.	CID 448003	UDA	**-12.4**	**-13.2**	**-13.0**	**-13.3**

4.4 Toxicity Report Of All The Inhibitors From ChemBio Server.

Table 56: Toxicity Report of all the Inhibitors

Sr. No.	PubChem ID	Report
1	CID 60855	Non-toxic
2	CID 58974096	Non-toxic
3	CID 59464423	Non-toxic
4	CID 60076457	Non-toxic
5	CID 71753010	Non-toxic
6	CID 448825	Non-toxic
7	CID 17754024	Non-toxic
8	CID 23422347	Non-toxic
9	CID 46936304	Non-toxic
10	CID 49852385	Non-toxic
11	CID 448003	Non-toxic

CHAPTER 5

CONCLUSION

5. CONCLUSION

DENV is able to infect many types of host cells and this resulted in the identification of several putative DENV receptors. DCs in the skin are believed to be the first target cells, and therefore DC SIGN is assumed to be the most important DENV receptor until now. Preventing the entry of DENV into the host cell can be a very good method to inhibit dengue fever. Carbohydrate Binding Agents(CBAs) are considered effective against inhibiting viral entry into the host cell. We selected such CBAs like *Hippeastrum hybrid* (HHA), *Galanthus nivalis* (GNA), and *Urtica dioica* (UDA), isolated from the amaryllis, snowdrop, and stinging nettle respectively, along with their analogues to check their binding energy with the CD209 isoforms using AutoDock vina. From the results, we can conclude that *Urtica dioica* (UDA) amongst all the inhibitors used have shown the least binding energy (-13.1 kcal/mol) and hence can be used as a potential drug in inhibiting DENV entry into the DCs and hence prevent dengue. These results prove that entry inhibitors can prove effective in developing drugs against dengue and hence this indicates a very important feature for further development of entry inhibitors and for future clinical studies.

6. REFERENCE

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